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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,492	03/06/2002	Elizabeth S. Light	142/003/PCT	8768

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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 01/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,492	LIGHT ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7 and 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This action is written in response to applicant's response to the office action submitted 11/26/03. Claims 1, 2, 3, 5, 6, and 7 have been amended, claims 4 and 8-16 have been canceled. Claims 1-6, 7, and 17-22 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Information Disclosure Statement

1. The information disclosure statement filed 12/2/03 fails to comply with 37 CFR 1.97(c) because it lacks the fee set forth in 37 CFR 1.17(p). It has been placed in the application file, but the information referred to therein has not been considered.

2. The information disclosure statement (IDS) submitted on 8/4/03 was filed after the mailing date of the first office action on 6/26/03. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-7 and 17-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to reagents for detecting human papilloma virus DNA in a cell sample which comprise a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Dependent claims included in the rejection recite particular HPV types which hybridize to the probes and particular probes which do not, recite that the probes are "full length,"and include specific concentrations of particular probes in the reagent. The claims do not set forth any particular sequences or structure for the probes, and in fact only identify the claimed nucleic acids in terms of their function. The genus of the claimed reagents, therefore, includes any probe which is specific to any HPV type that is known to cause cancer, a genus which includes hundreds of thousands of possible reagents. Even for claims which recite particular HPV types, these claims encompass any set of oligonucleotide probes which would hybridize specifically to the recited types. The claims which recite "full length" probes are themselves quite broad, since the definition of "full length" in the specification is inclusive of "sequence variations and shortening of the probe length (specification page 5)." From applicant's specification, Applicant appears to be in possession of a single probe combination which meets the functional limitations of the instant claims, that is a probe set that comprises six separate plasmids, with one plasmid containing the whole genome of a HPV type and the six types being 16, 18, 31, 33, 35, and 51, wherein types 18, 33, 25, and 51 are present at 0.5 nanograms per milliliter of solution and types 16 and 31 re present at 0.2 nanograms per milliliter of solution (see p. 13, example 3), since this is the only reagent demonstrated by applicant to specifically hybridize only to those "high risk" types of HPV

designated by Applicant, and not to "low risk" HPV, see Table 5. Thus, applicant has express possession of only one species in a genus which comprises hundreds of millions of different possibilities.

With regard to the written description, all of these claims encompass reagents comprising nucleic acid sequence different from those disclosed in the specific reagents which for which no written description is provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only a single reagent meeting the functional limitations of the claims is described, yet hundreds of thousands of possible reagents are encompassed by the claims. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of reagents modified from the single example given but possessing the functional characteristics required by the claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 5, and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Meijer *et al.* (WO 95/22626).

Meijer *et al.* teach a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. In particular, Meijer *et al.* teach a mixture of probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58, and that this mixture does not contain probes specific for a variety of "low risk" HPV types (p. 16, lines 15-23).

With regard to claim 5, these probes are considered "full length" because an entire probe is given, and Meijer *et al.* teach using the full length of the probe in the reagent. The claim does not further define "full length" and thus the broadest reasonable interpretation of the claim is given.

With regard to claim 6, which recites that the reagent is "consisting essentially of" DNA probes to HPV types 16, 18, 31, 33, 35 and 51, in accordance with MPEP 2111.03, this transitional language is being interpreted to be the equivalent of "comprising" as there has been no clear indication in the specification of what the basic and novel characteristics of the claimed invention actually are. Applicant has the burden of showing that the introduction of additional components would materially change the characteristics of applicant's invention. Furthermore, it is noted that Meijer *et al.* teach that in a preferred embodiment, all twelve listed HPV types are present, but also teaches that the probe cocktail can be present as two or more different probe mixtures, thus teaching smaller groupings of HPV probes (p. 18, lines 20-24).

6. Claims 1 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Troncone *et al.* (J. Clin. Pathol. 1992, Vol. 45:308-313).

Troncone *et al.* teach a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. In particular, Troncone *et al.* teach a cocktail of full length genomic probes that are specific to HPV types 16, 18, and 33 (p. 309, "NISH ON CERVICAL SMEARS").

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer *et al.* in view of Orth *et al.* (US 5981173).

Meijer *et al.* teach a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-

risk HPV DNA. In particular, Meijer *et al.* teach a mixture of probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58, and that this mixture does not contain proves specific for a variety of "low risk" HPV types (p. 16, lines 15-23). Meijer *et al.* further teach that it is advisable to add HPV 59 to the high risk reagent and suggest that the probe cocktail needs to be supplemented when new identified high risk HPVs are found (p. 16, line 26-p. 17, line 5).

Meijer *et al.* do not teach a reagent that hybridizes to HPV types 68 and 70.

Orth *et al.* teach the genomes of HPV68 and HPV70 and teach that they were cloned from cervical interepithelial neoplasia (ABSTRACT, and throughout). Orth *et al.* teach oligonucleotide probes for the detection of HPV types 68 and 70 (Col. 3, lines 34-44) and teach that these probes can be used in combination with probes derived from other HPV (Col. 3, lines 54-56).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included probes specific for HPV 68 and HPV 70 in the reagents taught by Meijer *et al.* The ordinary practitioner would have been motivated to include the probes to the additionally HPV types in order to follow the explicit guidance provided by Meijer *et al.* to include additional HPV probes for a more complete set of probes for detection of HPV that lead to high risk for the development of cancer.

10. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer *et al.* in view of Bauer *et al.* (US 5639871).

Meijer *et al.* teach a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. In particular, Meijer *et al.* teach a mixture of probes specific for HPV types 16,

18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58, and that this mixture does not contain proves specific for a variety of "low risk" HPV types (p. 16, lines 15-23). Meijer *et al.* further teach that it is advisable to add HPV 59 to the high risk reagent and suggest that the probe cocktail needs to be supplemented when new identified high risk HPVs are found (p. 16, line 26-p. 17, line 5).

Meijer *et al.* do not teach a reagent having probes in the concentrations given in claim 7. However, the optimization of hybridization assays by determining ideal probe concentrations was routine in the prior art at the time the invention was made, as is exemplified by Bauer *et al.* who teach "The optimal ration and concentration of probe fragments to be used in the hybridization are determined empirically (Col. 51, lines 60-63)."

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have experimented with different probe concentrations so as to arrive at an optimal concentration for the detection of HPV in a sample. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52 ; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586 . Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372 ; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204 . However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433 ; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308 ; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314 . More

> particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412 ; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213 ; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

For these reasons, the claimed invention is *prima facie* obvious.

11. Claims 17, 18, 20, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer *et al.* in view of the 1988 Stratagene Catalog.

Meijer *et al.* teach a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. In particular, Meijer *et al.* teach a mixture of probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58, and that this mixture does not contain proves specific for a variety of "low risk" HPV types (p. 16, lines 15-23).

With regard to claim 5, these probes are considered "full length" because an entire probe is given, and Meijer *et al.* teach using the full length of the probe in the reagent. The claim does not further define "full length" and thus the broadest reasonable interpretation of the claim is given.

With regard to claim 6, which recites that the reagent is "consisting essentially of" DNA probes to HPV types 16, 18, 31, 33, 35 and 51, in accordance with MPEP 2111.03, this transitional language is being interpreted to be the equivalent of "comprising" as there has been no clear indication in the specification of what the basic and novel characteristics of the claimed invention actually are. Applicant has the burden of showing that the introduction of additional components would materially change the characteristics of applicant's invention. Furthermore, it is noted that Meijer *et al.* teach that in a preferred embodiment, all twelve listed HPV types are

present, but also teaches that the probe cocktail can be present as two or more different probe mixtures, thus teaching smaller groupings of HPV probes (p. 18, lines 20-24).

Meijer *et al.* do not teach kits wherein the reagents are in containers.

Stratagene teaches gene characterization kits. The ordinary practitioner would have been motivated to have produced such a kit because since the Stratagene catalog expressly teaches the benefits to the practitioner of kits:

> "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, pre-mixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control."

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at tee time the invention was made to have packaged the reagents taught by Meijer *et al.* into containers for distribution in a kit. The ordinary practitioner would have been motivated to provide such kits in order to provide consumers with the convenience of kits for the detection of HPV in samples, since Stratagene expressly describes the benefits of such kits. Therefore, the kits of the instant claims are *prima facie* obvious over the disclosure of Meijer *et al.* in view of the Stratagene catalog.

12. Claims 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Troncone *et al.* in view of Stratagene 1988 Catalog.

Troncone *et al.* teach a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-

risk HPV DNA. In particular, Troncone *et al.* teach a cocktail of full length genomic probes that are specific to HPV types 16, 18, and 33 (p. 309, "NISH ON CERVICAL SMEARS").

Troncone *et al.* do not teach kits wherein the reagents are in containers.

Stratagene teaches gene characterization kits. The ordinary practitioner would have been motivated to have produced such a kit because since the Stratagene catalog expressly teaches the benefits to the practitioner of kits:

> "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, pre-mixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control."

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at tee time the invention was made to have packaged the reagents taught by Troncone *et al.* into containers for distribution in a kit. The ordinary practitioner would have been motivated to provide such kits in order to provide consumers with the convenience of kits for the detection of HPV in samples, since Stratagene expressly describes the benefits of such kits. Therefore, the kits of the instant claims are *prima facie* obvious over the disclosure of Troncone *et al.* in view of the Stratagene catalog.

13. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer *et al.* in view of Orth *et al.* as applied to claim 3 above, and further in view of Stratagene 1988 catalog.

The particular teachings of Meijer *et al.* in view of Orth *et al.* with respect to claim 3 are set forth in the previous rejection. Meijer *et al.* in view of Orth *et al.* further do not teach kits wherein the reagents are in containers..

Stratagene teaches gene characterization kits. The ordinary practitioner would have been motivated to have produced such a kit because since the Stratagene catalog expressly teaches the benefits to the practitioner of kits:

> "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, pre-mixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control."

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents taught by Meijer *et al.* in view of Orth *et al.* into containers for distribution in a kit. The ordinary practitioner would have been motivated to provide such kits in order to provide consumers with the convenience of kits for the detection of HPV in samples, since Stratagene expressly describes the benefits of such kits. Therefore, the kits of the instant claims are *prima facie* obvious over the disclosure of Meijer *et al.* in view of Orth *et al.* and further in view of the Stratagene catalog.

14. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer *et al.* in view of Bauer *et al.* as applied to claim 7 above, and further in view of Stratagene 1988 catalog.

The particular teachings of Meijer *et al.* in view of Bauer *et al.* with respect to claim 7 are set forth in the previous rejection. Meijer *et al.* in view of Bauer *et al.* further do not teach kits wherein the reagents are in containers.

Stratagene teaches gene characterization kits. The ordinary practitioner would have been motivated to have produced such a kit because since the Stratagene catalog expressly teaches the benefits to the practitioner of kits:

> "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, pre-mixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control."

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents taught by Meijer *et al.* in view of Bauer *et al.* into containers for distribution in a kit. The ordinary practitioner would have been motivated to provide such kits in order to provide consumers with the convenience of kits for the detection of HPV in samples, since Stratagene expressly describes the benefits of such kits. Therefore, the kits of the instant claims are *prima facie* obvious over the disclosure of Meijer *et al.* in view of Bauer *et al.* and further in view of the Stratagene catalog.

15. Claims 1, 2, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer *et al.* in view of Faulkner-Jones *et al.*

This rejection is written to address an interpretation of "viral genomic HPV DNA probes" in which the genomic HPV DNA probes are entire HPV genomes, and thus is necessitated by applicant's amendments to the claims.

Meijer *et al.* teach a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. In particular, Meijer *et al.* teach a mixture of probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58, and that this mixture does not contain probes specific for a variety of "low risk" HPV types (p. 16, lines 15-23).

With regard to claim 5, these probes are considered "full length" because an entire probe is given, and Meijer *et al.* teach using the full length of the probe in the reagent. The claim does not further define "full length" and thus the broadest reasonable interpretation of the claim is given.

With regard to claim 6, which recites that the reagent is "consisting essentially of" DNA probes to HPV types 16, 18, 31, 33, 35 and 51, in accordance with MPEP 2111.03, this transitional language is being interpreted to be the equivalent of "comprising" as there has been no clear indication in the specification of what the basic and novel characteristics of the claimed invention actually are. Applicant has the burden of showing that the introduction of additional components would materially change the characteristics of applicant's invention. Furthermore, it is noted that Meijer *et al.* teach that in a preferred embodiment, all twelve listed HPV types are present, but also teaches that the probe cocktail can be present as two or more different probe mixtures, thus teaching smaller groupings of HPV probes (p. 18, lines 20-24).

Meijer *et al.* do not teach a reagent in which the probes are "viral genomic HPV DNA probes" in which the genomic HPV DNA probes are entire HPV genomes.

Faulkner-Jones *et al.* teach reagents for detecting HPV in samples, and specifically teach methods for isolating whole genomic probes (p. 280). Faulkner-Jones *et al.* (Journal of Virological Methods, 41 (1993) 277-296) teach that for DNA detection the use of full length genomic probes is preferred over oligonucleotide probes because full length genomic probes are more sensitive.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the reagent taught by Meijer *et al.* so as to have provided a reagent comprising whole genomic probes as taught by Faulkner-Jones *et al.* One would have been motivated to use the whole genome HPV probes taught by Faulkner-Jones *et al.* in order to produce a probe cocktail with increased sensitivity for DNA detection, as Faulkner-Jones *et al.* specifically teach that "The sensitivity of the oligonucleotide probes for the detection of HPV DNA as assessed by dot blot, was generally less than the full genomic probes in this study (p. 292)." And thus, one would have been motivated to have provided a reagent comprising whole genome probes in order to have provided a reagent that is more sensitive for the detection of HPV DNA.

16. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer *et al.* in view of Faulkner-Jones *et al.* as applied to claims 1, 2, 5, and 6 above, and further in view of Orth *et al.*

The teachings of Meijer *et al.* in view of Faulkner-Jones *et al.* are discussed previously.

Meijer *et al.* in view of Faulkner-Jones *et al.* do not teach a reagent that hybridizes to HPV types 68 and 70.

Orth *et al.* teach the genomes of HPV68 and HPV70 and teach that they were cloned from cervical interepithelial neoplasia (ABSTRACT, and throughout). Orth *et al.* teach the cloning of the entire genome of these HPV types.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included probes specific for HPV 68 and HPV 70 in the reagents taught by Meijer *et al.* in view of Faulkner-Jones *et al.* The ordinary practitioner would have been motivated to include the probes to the additionally HPV types in order to follow the explicit guidance provided by Meijer *et al.* to include additional HPV probes for a more complete set of probes for detection of HPV that lead to high risk for the development of cancer.

17. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer *et al.* in view of Faulkner-Jones *et al.* as applied to claims 1, 2, 5, and 6 above, and further in view of Bauer *et al.* (US 5639871).

The teachings of Meijer *et al.* in view of Faulkner-Jones *et al.* are discussed previously.

Meijer *et al.* in view of Faulkner-Jones *et al.* do not teach a reagent having probes in the concentrations given in claim 7. However, the optimization of hybridization assays by determining ideal probe concentrations was routine in the prior art at the time the invention was made, as is exemplified by Bauer *et al.* who teach "The optimal ration and concentration of probe fragments to be used in the hybridization are determined empirically (Col. 51, lines 60-63)."

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have experimented with different probe concentrations so as to arrive at an optimal concentration for the detection of HPV in a sample. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52 ; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586 . Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372 ; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204 . However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433 ; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308 ; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314 . More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412 ; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213 ; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

For these reasons, the claimed invention is *prima facie* obvious.

Response to Remarks

The 112 2nd rejections of the previous office action are withdrawn in view of applicant's amendments to the claims.

With regard to the 112 1st paragraph rejection, applicant points out that claim 1 has been amended to recite "viral genomic HPV DNA probes," and points out that the specification

describes the HPV probes as "essentially full length genomic HPV probes," providing examples of sequences known in the prior art that are within the scope of the claimed invention. However, it is noted that first, the independent claim, while reciting that the probes are "genomic" does not recite that the probes are probes of any length. Limitations from the specification are not read into the claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. Thus, as discussed in the Written Description rejection, there are many, many different probes of many, many lengths that are encompassed within the rejected claims. Though the specification generically states that the probes "are not similar to oligonucleotide probes as used in the prior art (p. 5, first paragraph)" this specification does not clearly distinguish from which oligonucleotide probes or what is considered an "oligonucleotide" versus a "genomic" probe. In light of the broad nature of the claims, the written description rejection is maintained.

In arguing against the prior art rejections, applicant is again relying on the amendment of the claims to recite "viral genomic HPV DNA probes" to distinguish the claimed invention from the invention of the prior art. However, this is not persuasive. The probes taught by Meijer *et al.* are genomic probes, that is they would hybridize to portions of the genome. With the exception of claim 5, none of the rejected claims even recite that the probes of the claimed invention are "full length HPV probes." With regard to claim 5, as noted in the rejection, even the recitation "full length HPV probes" is not sufficiently limiting because there is no clear definition of this language in the specification. Again it is noted that by quoting the specification in the arguments, applicant is attempting to read limitations from the specification into the claims. In response to applicant's argument that the references fail to show certain features of applicant's

invention, it is noted that the features upon which applicant relies (i.e., length limitations of the probes) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant is attempting to confer a specific definition on the claimed probes based on the language "genomic" versus "oligonucleotide," however, these definitions are not supported in the specification. The probes taught by Meijer *et al.*, as previously noted, would hybridize to genomic HPV DNA, and are therefore fairly considered "genomic" probes.

Applicants point out that the probes taught by Meijer *et al.* comprise only about 30 nucleotides, and therefore are not full length probes. However, it is noted that claim 5 does not recite that the probes cover the full length of the HPV genome, only that the probes themselves are "full length." As discussed in the rejection, the probes taught by Meijer *et al.* meet this limitation. The rejection of Meijer *et al.* is maintained over an interpretation of "genomic" probe which requires that the probes hybridize to genomic DNA, which the probes taught by Meijer *et al.* would do.

With regard to the Trocone *et al.* reference, applicant's interpretation of the reference is not the same as the examiner's. It is agreed that Trocone *et al.* disclose a NISH study in which samples were first analyzed in separate hybridizations with "genomic HPV probes." These samples were histopathological sections, and, as stated by applicant, none of these were positive for types 6 or 11. Applicant then states that samples were re-examined by hybridization with a cocktail of probes. However, for clarification, it is noted that different samples were examined with the cocktail of probes, and it is not clear why Trocone *et al.* used the cocktail of probes that

they selected. The samples were taken from the same individuals, but the first samples are histopathological samples, while the second samples were from cervical smears (p. 309). Nonetheless, the fact remains, that Trocone *et al.* teach a cocktail of probes that comprises probes for HPV types 16, 18, and 33, each of which are carcinogenic HPV types.

Applicants contend that it is not clear from the reference that the 16/18/33 cocktail of Troncone *et al.* specifically hybridizes to only carcinogenic HPV types because in the samples that were tested using the cocktail, no non-carcinogenic HPV types were detected. This is not persuasive. First, the samples that were tested using the cocktail were not tested using probes to non-carcinogenic types. Thus, no detection was even possible. It is clear from the teachings of Troncone *et al.*, that they are using these probes to specifically detect the 16/18/33 types of HPV, and these are indisputably carcinogenic HPV types (as supported in fact by even applicant's own specification). Applicant does not provide any evidence that these probes would hybridize to non-carcinogenic types. MPEP 716.01(c) makes clear that

> "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

Applicant further argues that it is not clear that the probes used by Troncone *et al.* are genomic probes as opposed to oligonucleotide probes. It is noted that an oligonucleotide is a compound that has more than one nucleotide, but there is no inherent length limitation imparted by the use of this term. The probes taught by Trocone *et al.* are considered genomic probes because they would hybridize to genomic HPV DNA. It is not clear what further distinction is

imparted by the phrase "genomic probe." Furthermore, the teachings of Trocone *et al.* specifically teach that genomic probes are used in the NISH of histopathological samples, and it follows from the teaching that genomic probes are being used on the subsequently tested cervical smears, an argument that is supported by the fact that Trocone *et al.* utilize the same detection method on the smears and on the sections (p. 309, second column).

Conclusion

18. No claims are allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached by calling (571) 272-0782.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

JEFFREY FREDMAN
PRIMARY EXAMINER

Juliet C Switzer
Examiner
Art Unit 1634

January 21, 2004